

REMARKS

Status of the Claims.

Claims 1, 3-19, and 21-32 are pending with entry of this amendment, claims 2 and 20 being cancelled and no claims being added.

35 U.S.C. §112, First Paragraph, Description requirement.

Claims 1-32 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) at the time the application was filed, had possession of the claimed invention (description requirement).

The Examiner alleges that Applicants fail to show a correlation between function and structure with respect to the claimed lyase domain. In addition, the Examiner alleges that the claims encompass variations and derivatives including substitutions, insertions or deletions of any amino acid without limitation. The Examiner further alleges that the art is unpredictable and even a single amino acid change can destroy the function of the biomolecule. With respect to Cph1, Cph2, Cph3, Cph4, Cph5, Cph6, Cph7, and Cph8 the Examiner alleges that these sequences are greater than 400 amino acid long and are not representative of apoproteins that are of about 190 to 400 amino acids.

Applicants traverse.

It is well accepted law that the description requirement of section 112 is met when "one of skill in the art would discern possession of the invention at the time of filing." As stated by the Court of Appeals of the Federal Circuit:

After Enzo, this court recognized "that Ely Lilly did not hold that all functional descriptions of genetic material necessarily fails as a matter of law to meet the written description requirement, rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." Amgen, 314 F.3d at 1332, 1361 (dissent: "[T]he majority . . . verges on confining Ely Lilly to its facts.").

In this case, as in Enzo, the court explained that the written description requirement is satisfied when "one of skill in the art would discern possession of the invention at the time of filing." [emphasis added] (Moba,

B.V., Staalkat, B.V., And Fps Food Processing Systems, Inc., V. Diamond Automation, Inc., ___USPQ2d ___(Fed. Cir. 2003).

The Examiner is simply incorrect in her assertion that Cph1 through Cph8 are not examples of apoproteins that are of about 190 to 400 amino acids that comprise lyase activity. As states in the specification with reference to these sequences:

Underlining in each sequence indicates location of the chromophore domain. Potential cysteine attachment sites are indicated in boldface. [emphasis added] (page 40, lines 2-3).

Moreover, the specificalton expressly states:

The terms "chromophore domain" or "minimal chromophore domain" or "lyase domain" refer to the apoprotein N-terminal subsequence sufficient for lyase activity and thereby form a covalent bond between the apoprotein and the bilin.

Using the sequence information provided, an N-terminal sequence comprising a lyase domain is clearly delineated. Thus for example, an N terminal sequence of Cph1 containing a lyase domain is:

MATTVQLSDQSLRQLET LAIHTAHLIQPHGLVVVLQEPDLTISQISANC
TGILGRSPEDLLGRTLGEVFD SFQIDPIQSRLTAGQISSLNPSKLWARV
MGDDFVIFDGVFHRNSDGLLVCELEPAYTSDNLPFLGFYHMANAAL
NRLRQQANLRDFYDVIVEEVRRTMGFDRVMLYRFDENNHGDVIAED
KRDDMEPYLGLHYPESDIPQARRLFHNP IRVIPDVYGVAVPLTPAV
NPSTNRAVDLTESILRSAYHCHLTYLKNMGVGASLTISLIKDGHLWG
LIACHHQTPKVIPFELRKACEFFGRVVFSNISAQEDTETFDIRV

This sequence is 329 amino acids in length. Similarly, an N terminal sequence of Cph2 containing a lyase domain is:

MNPNRSLEDFLRNVINKFHRALTLRETLOVIVEEARIFLGVDRVKIYK
FASDGSGEVLAEAVNRAALPSLLGLHFPVEDIPQAREELGNQRKMIA
VDVAHRRKKSHELSGRISPTESNGHYTTVDSCHIQYLLAMGVLSSL
TVPVMQDQQLWGIMAVHHSKPRRFTEQEWETMALLSKEVSLAITQS
QLSRQ

This sequence is 194 amino acids in length. Similar determinations can readily be made for Cph3-Cph8.

Thus, the Examiner is incorrect in her assertion that the listed sequences are not representative examples of apoproteins that are of about 190 to 400 amino acids that comprise lyase activity.

Moreover, it is well known that phytochromes consist of a highly conserved N-terminal polypeptide. As stated in the specification:

Phytochromes from cyanobacteria, to green algae and higher plants consist of a well conserved N-terminal polypeptide, roughly 390-600 amino acids in length (see Figure 6 of WO 98/04700), to which the bilin prosthetic group phytochromobilin (PΦB) or phycocyanobilin (PCB) is bound. [emphasis added] (page 1, lines 21-24).

Since:

- 1) All phytochromes comprise an attached bilin;
- 2) Bilin attachment is accomplished by lyase activity of the phytochrome; and
- 3) Lyase activity has been shown to reside in a highly conserved N-terminal portion of the apoprotein comprising the phytochrome;

One of skill would readily recognize and accept that the lyase domain of a phytochrome can readily be identified, *e.g.* by a sequence alignment with phytochromes in which the lyase domain is known.

Figure 2 in the present application shows such a multiple sequence alignment of the chromophore (lyase) domains of representative eukaryotic phytochromes the Arabidopsis (At) phyA, phyB/D, phyC and phyE proteins and the green algal phytochrome (McpHy1b) and the cyanobacterial phytochrome sequences of the invention, cph1-2 and cpl1-6."

Thus, contrary to the Examiners assertion, the specification shows numerous examples of the claimed invention:

- | | |
|---------|------------|
| 1) Cph1 | 9) AtphyA |
| 2) Cph2 | 10) AtphyB |
| 3) Cph3 | 11) AtphyC |
| 4) Cph4 | 12) AtphyD |

- | | |
|----------|-------------|
| 5) Cph5 | 13) AtphyE |
| 6) Cph6, | 14) Mcphy1b |
| 7) Cph7 | |
| 9) Cph8 | |

Moreover, the Examiner's assertions regarding unpredictability of the art and possible inoperable embodiments, are simply not germane to the question of written description under 35 U.S.C. §112, first paragraph. The Examiner is reminded that a claim need not exclude possible inoperable embodiments. As stated by the PTO Board of Appeals:

It is always possible to theorize some combination of circumstances which would render a claimed composition or method inoperative, but the art-skilled would assuredly not choose such a combination. *Ex parte* Cole, 223 USPQ 94 (BPAI 1983)

Similarly, the Federal Circuit has stated that

It is not the function of claims to specifically exclude either possible inoperative substances or ineffective reactant proportions. *In re Dinh-Nguyen and Stenhagen*, 181 USPQ 46 (CCPA 1974)

For a proposed claim to be unpatentable, the law requires that the number of inoperable embodiments be significant in numbers **and not readily ascertained** by those of skill. *In re Cook and Merigold*, 169 USPQ 298, 301-302 (CCPA, 1971).

In the present case, particularly given the highly conserved nature of phytochrome apoproteins, operable embodiments, are readily created (*e.g.* using the multiple sequence alignments). Moreover, **inoperable embodiments are readily ascertained** -- lacking lyase activity; they will not bind a bilin. It is also noted that such inoperable embodiments, are **expressly excluded** by the claims.

Having reduced to practice **fourteen species** comprising each of the major groups recited in claims 1 and 17 (as amended herein) and having provided a multiple sequence alignment of these chromophore (lyase) domains, one of ordinary skill in the art would readily appreciate that Applicants were in possession of the claimed invention at the time of filing. Accordingly, Applicants

believe they have met the description requirement of 35 U.S.C. §112, first paragraph and respectfully request that this rejection be withdrawn.

If the Examiner wishes to maintain this rejection, he is requested to identify for the record, just how many species he believes would be required to support the presently pending claims.

Moreover, if the Examiner wishes to maintain this rejection Applicants expressly request a telephone interview with the Examiner and the Examiner's supervisor to discuss this matter.

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. Should the Examiner seek to maintain the rejections, Applicants request a telephone interview with the Examiner and the Examiner's supervisor.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 769-3513.

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Respectfully submitted,



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